REMARKS

Applicants wish to thank the Examiner for withdrawing the finality of the Office Action mailed on May 7, 2002. Applicants also wish to thank the Examiner for withdrawing the §112 new matter rejection. Claims 18-34 are pending. Claim 18 has been amended. The claims as amended now recite compositions of MBL binding peptides which have an MBL CDR3 region or functional variants thereof, wherein the functional variants contain an MBL binding CDR3 region with conservative substitutions therein. No new matter has been added.

Rejection of Claims 18-29, 33 and 34 Under 35 U.S.C. § 112, First Paragraph

The Examiner has maintained the rejection of claims 18-29, 33 and 34 under 35 U.S.C. § 112, first paragraph, as containing subject matter not described in a way to reasonably convey to one of skill in the art that the Applicants, at the time the application was filed, had possession of the claimed invention. The Examiner asserts that "one would not know if they were in possession of a species of the genus of functional variants of the recited core protein because the specification does not provide a structural basis for the location, or the number or the type of substitutions, additions and deletions in the core peptide that could be made and still function as an MBL inhibitor."

Claim 18 has been amended to recite compositions of MBL binding peptides which include functional variants which bind MBL and contain an MBL CDR3 region with conservative substitutions therein. Thus, the claim now recites a structural basis to alter the core peptide and produce the MBL binding functional variants. The disclosure further provides a representative number of functional variants with the recitation of the suggested modifications found on page 19, line 23-31. The recitation of these possible conservative substitutions in conjunction with the deposited antibodies, from which the sequence of the CDR3 regions are easily determined, is sufficient to demonstrate Applicants were in possession of the claimed MBL binding functional variants.

Based on the foregoing, the specification provides an adequate description of the invention to demonstrate that Applicants had possession of the claimed invention. The Applicants respectfully request that the rejection of claims 18-29, 33 and 34 under 35 U.S.C. §

112, first paragraph be withdrawn in view of the claim amendment and arguments presented above.

Rejection of Claims 18-29, 33 and 34 Under 35 U.S.C. 112, First Paragraph

The Examiner has rejected claims 18-29, 33 and 34 under 35 U.S.C. 112, first paragraph, as not reasonably providing enablement for the recitation of a "composition comprising an MBL inhibitor comprising any peptide comprising an MBL CDR3 region of said antibodies, or any functional derivative thereof." The Examiner maintains that one of skill in the art would not be able to practice the invention as broadly as claimed.

The Examiner correctly points out that the instant claims encompass six CDR3 regions (two CDR3 regions from each of the three antibodies produced from the three deposited hybridomas). However, the Applicants maintain that the claims as amended, to MBL binding peptides that contain a CDR3 region or a functional variant thereof, wherein the functional variant contains a conservative substitution therein, are sufficiently enabled. The specification and level of skill in the art provide sufficient guidance for one of ordinary skill to make and test the MBL binding peptides of the claims.

Janeway et al.

The Examiner notes that the "specification does not exemplify the ability of any peptide consisting of one of the six CDR3 peptides as inhibiting complement activation." The Applicants contend, however, that they are not required to do so. The Applicants maintain that an absence of working examples is not dispositive to the enablement of the claimed methods. A working example need not be provided if the invention is otherwise disclosed in a manner such that one of ordinary skill would be able to practice the invention without undue experimentation. Applicants maintain that with the guidance provided as well as the high level of skill in the art, this is the case.

The Applicants briefly reiterate that one of skill would know how to make a peptide comprising one of the CDR3 regions of the antibodies produced from the deposited hybridomas and determine whether or not the peptide selectively binds a human MBL epitope. The Applicants provide three deposited hybridomas (3F8, 2A9 and hMBL1.2). One of skill would

know how to produce the antibodies from the deposited hybridomas with routine methods known in the art. One of skill would know how to produce fragments of these antibodies, also with routine methods. One of skill would know how to determine the sequence of a CDR3 region of these antibodies (see page 27). One of skill would recognize how to synthesize and/or isolate peptides containing such a CDR3 region with routine methods. One of skill would also know how to produce functional variants of the peptides containing a CDR3 region (a list of conservative substitutions are provided on page 19, lines 29-30.) Additionally, one of skill is also able to assess the function of the peptides produced (binding assays and competition assays are provided on pages 16-17).

The Examiner further notes that the antibody specificity is determined by the CDR1, CDR2 and CDR3 regions of both antibody chains (heavy and light). The Applicants, however, contend that this teaching does not demonstrate that one of ordinary skill in the art would be unable to make and test the peptides of the amended claims or would need to resort to undue experimentation, even those which consist of an MBL binding CDR3 region. The Applicants assert that Janeway et al. does not teach that peptides which consist of a CDR3 region would be expected to fail to selectively bind to a human MBL epitope. Janeway et al., in fact, describes the importance of the CDR3 regions for antibody specificity. To this the Examiner has already agreed. The Applicants, therefore, assert that, without teachings to the contrary, a peptide which consists of a CDR3 region would be expected to selectively bind MBL. That other regions might further contribute partially to binding is not a teaching that a CDR3 peptide will not selectively bind. Furthermore, as argued above, one of ordinary skill in the art would know how to make a peptide with a CDR3 region and determine the peptide's ability to bind a human MBL epitope using only routine methods known in the art and the teachings of the specification. Applicants, in fact, provide a number of examples of peptides encompassed by the amended claims (i.e. the intact soluble antibodies produced from the deposited hybridomas, fragments of these antibodies (e.g. $F(ab')_2$, F(ab), etc.), functional variants, etc.). Applicants, therefore, maintain that with the guidance provided and high level of skill in the art, one of ordinary skill in the art would be sufficiently enabled to make an isolated MBL binding peptide with a CDR3 region or functional variant thereof which selectively binds to a human MBL epitope.

The Applicants also assert that the level of skill in the art has an important effect on the amount of guidance which must be provided to enable the inventions. As the court stated in *In re Howarth*, "[i]n exchange for the patent, [the applicant] must enable other to practice his invention. An inventor need not, however, explain every detail since he is speaking to those skilled in the art." *In re Howarth*, 654 F.2d 103, 105 (CCPA 1981). Moreover, one of ordinary skill in the art is accustomed to complex experimentation, and thus the experimentation required to make and use the claimed invention would be considered routine to the ordinary artisan. Based on the high level of skill and the experimentation that is routinely performed in the art, one of ordinary skill would be able to make, test and use the isolated MBL binding peptides and, therefore, be able to practice the claimed invention without undue experimentation.

Additionally, for the level of experimentation to be undue, it must be demonstrated that the experimentation is more than typically engaged in in the art. Requiring complex or even a large amount of experimentation is not sufficient to make it undue, if the art routinely engages in this level of experimentation. Applicants assert that this level of experimentation is typically engaged in in the art, and accordingly this kind of experimentation is routine and not undue.

Abaza et al.

Regarding the predictability of amino acid substitutions to produce the functional variants of the amended claims, the Examiner maintains that even though Abaza et al. teaches amino acid changes in an antigen outside of its epitope, because these changes effected the ability of antibody to bind antigen, these teachings "denote the unpredictability of changing amino acids within the antigen antibody binding site."

The Applicants, however, respectfully disagree. Not only do the amino acid substitutions of the functional variants taught by the Applicants occur within the CDR3 region of the antibody, but the kind of amino acid substitutions are also different. Specifically, the amino acid substitutions of Abaza et al. are those which are taught to result in conformational changes in the antigen which alter the binding of the antigen to an antibody. However, amino acid substitutions made to produce the functional variants of the amended claims are not those which result in large-scale conformational changes but rather are conservative substitutions as described in the specification on page 19. Therefore, the teachings in Abaza et al. are not relevant to the

predictable nature of conservative substitutions of a CDR3 region contained in an MBL binding peptide.

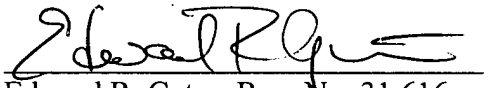
In view of the forgoing, one of ordinary skill in the art is enabled to practice the claimed invention. Applicants therefore, respectfully request the Examiner withdraw the rejections under 35 U.S.C. §112, first paragraph.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the rejections. This application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes after this Amendment that the application is not in condition for allowance, the Examiner is requested to call the Applicants' attorney at the number requested below.

Respectfully submitted,

Gregory L. Stahl et al., Applicant(s)

By: 

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MARKED-UP CLAIM

18. (Thrice Amended) A composition, comprising an [MBL inhibitor, wherein the MBL inhibitor is an]isolated binding peptide that selectively binds to a human MBL epitope[and that inhibits LCP associated complement activation], wherein the isolated MBL binding peptide has an MBL binding CDR3 region or a functional variant thereof of a monoclonal antibody produced by a hybridoma cell line selected from the group consisting of hybridoma cell line$_{(3F8)}$ hybridoma cell line$_{(2A9)}$, and hybridoma cell line$_{(hMBL1.2)}$ deposited under ATCC accession numbers HB-12621, HB-12620, and HB-12619 respectively, and wherein the functional variant thereof has an MBL binding CDR3 region with a conservative substitution therein.